REMARKS

Claims 9, 14, 16-22 and 24 are pending in this application. Applicants cancel claim 23 without prejudice or disclaimer. Applicants have amended claims 9 and 24. Support for the amendment to claim 9 can be found at page 7, lines 35-45; Examples 1, 4-9; and original claims 2 and 3. Support for the amendment to claim 24 can be found at page 11, lines 15-26; page 12, lines 10-16; page 13, lines 15-22; and Examples 4 and 5. Therefore, no new matter has been added. The Office Action is discussed below:

Written Description Rejection:

Without acquiescing in the rejection, applicants submit that the amendment to claim 9 by adding a recitation of a particular activity, such as complement inhibitory, moots the rejection.

Regarding claim 24, applicants respectfully disagree with the examiner's allegation that the identification/description of the Soltran solution is indefinite. Applicants refer to the composition of the solution as described in the specification (see for example, page 11, lines 15-26). The composition also is described as a "kidney perfusion solution" throughout the specification (see for example, page 12, lines 10-16; page 13, lines 15-22; page 25 Example 4; and page 26 Example 5). However, without acquiescing in the rejection, applicants amend the claim to recite "kidney perfusion solution" and the trade name "SOLTRAN" in parenthesis to identify the source of the perfusion solution (see for example, page 11, lines 15-16). Withdrawal of the rejection is therefore solicited.

Anticipation Rejection:

On pages 4-5 of the office action, the examiner has repeated the rejection of the claims allegedly as being anticipated by both Rittershaus *et al.* (U.S. Patent No.

6,193,979) and Smith *et al.,* (U.S. Patent No. 6,713,606). Applicants respectfully disagree with the examiner and traverse the rejection.

Applicants reiterate that "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). *See* MPEP § 2131.01 (Rev. 5, August 2006). Applicants review below the references with these concepts in mind.

As explained previously, the Rittershaus relates to a composition comprising complement proteins related to the complement receptor type 1 (CR1) and preferably in combination with the Lewis X antigen or the sialyl Lewis X antigen (see column 1, lines 16-25). Rittershaus *et al.* refer to forms of soluble CR1 (sCR1), wherein the polypeptide chain contains modified glycoforms (including Le^x and sialyl Le^x) (see for example, col. 9, lines 58-66), which are not intrinsically membrane-interactive. The compositions of Rittershaus *et al.* mediate binding to membranes only if a protein (*e.g.*, E-selectin), for which these glycoform modifications are ligands, is expressed in a membrane-bound form on cells. Importantly, Rittershaus does not disclose

> at least two membrane binding elements, wherein (a) at least one membrane binding element is a non-peptidic membrane binding element comprising acyl groups, and (b) at least one membrane binding element is a peptidic membrane binding element comprising basic amino acids, wherein the peptidic membrane binding element is bound to the non-peptidic membrane binding element and the fragment of complement receptor 1....

In contrast, the claimed methodology employs soluble derivatives that comprise at least two such binding elements and therefore intrinsically can bind to any cell membrane, and are not dependent on the presence of an up-regulated protein for

binding. This allows delivery and retention of very high levels of a complement regulatory molecule to an organ.

Applicants also wish to remind the examiner that Rittershaus *et al.* disclosed a CR1 protein which was not the CR1 fragment recited in the claims, but was modified by glycoform manipulation. Such modification is not possible for SEQ ID NO:1, which differs from Rittershaus' protein because, among other things, SEQ ID NO:1 lacks a single N-linked glycosylation site from which a sialyl Le^x structure could be attached. Thus, even if the composition of Rittershaus *et al.* were to be retained in ischemic organs, which the examiner has not demonstrated, such a molecule could not be derived from the region of CR1 utilized in the instant invention. In sum, because Rittershaus does not disclose the same type of molecule as is claimed, this reference cannot anticipate the claims.

Turning to Smith, this patent discloses soluble derivatives of soluble peptides that can be used according to the invention. The present claims, however, are not solely directed to such composition or derivatives, but rather inventive methods of use for the soluble derivatives. Such claims are specifically permitted under 35 USC §§ 100(b), 101. These methods require the presence of the soluble derivative in an isolated organ. Accordingly, the invention claimed here requires the organ to be in an *ex vivo* environment, which precedes transplantation. The Smith patent does not concern organ removal to an *ex vivo* environment, and certainly all medical practitioners, as well as patients, would not consider organ removal for transplantation to be an implicit or obvious extension of other therapeutic treatments, which do not involve *ex vivo* environments. Therefore, withdrawal of the anticipation rejection is requested.

On page 7 of the Office Action, in response to the arguments submitted on April 13, 2006, the examiner asserted that "because the structure of CR1 disclosed by Rittershaus *et al.* is the same as the structure of the protein in the instant invention", Rittershaus *et al.* would anticipate the claims as written. Applicants respectfully

disagree with the examiner and refer to above clarification distinguishing the Rittershaus *et al.* Applicants also point out that the claims are directed to a "method for preparing an organ by perfusion prior to transplantation or storage" and not to the structure as alleged by the examiner.

Regarding Smith *et al.*, applicants also refer to above clarification distinguishing the Smith *et al.* and point out that the claims are directed to a "method for preparing an organ by perfusion prior to transplantation or storage" and not solely to the membrane binding elements or polypeptides as alleged by the examiner.

Moreover, applicants herewith provide a copy of the recently published article (see enclosed Patel *et al. J Am Soc Nephrol,* 2006 April 17(4):1102-1111) that highlights the beneficial effects of having a soluble derivative (for example, APT070) in a composition for prevention of ischemic reperfusion injury, according to the claimed invention. For example, see Patel *et al.* pages 1106-1109 (more specifically, see p.1106, right column) that discloses the finding that pretreatment of donor kidney with APT070 increases the number of usable donor organs (see Patel *et al.*, Figures 5-6, for example). The publication of Patel *et al.* in *J Am Soc Nephrol.* further supports the fact that the claimed invention is novel and a technological advance over what was known in the art.

Accordingly, applicants respectfully request withdrawal of the anticipation rejection.

Obviousness Rejection:

On pages 5-6 and the paragraph bridging pages 7-8 of the office action, the examiner has repeated the rejection of the claims 9, 14, and 16-21, under 35 USC § 103, allegedly as being unpatentable over Rittershaus in view of Smith. In sum, the examiner seeks to reconstruct Rittershaus by substituting Rittershaus' compound with the compounds of the Smith patent. The examiner, however, has provided no factually-supported rationale for performing a method that would require substituting Rittershaus'

transplant compound with the compound of the Smith patent when the Smith patent says nothing about the use of its compounds in a transplantation (*ex vivo*) environment. As stated above, organ removal for transplantation is very different from other therapeutic regimens in that organ transplantation involves the *ex vivo* environment and the movement of an organ from one subject to another with typically a storage step in between. This complex medical procedure is not implicated in any way by the examiner's citation to the mere mention of "post-ischemic reperfusion injuries". Applicants therefore reiterate that the examiner has undertaken a proscribed hindsight reconstruction of the prior art, and therefore has not established a *prima facie* case of obviousness. Accordingly, applicants respectfully submit that the rejection should be withdrawn.

Miscellaneous:

On page 1 section 1) and page 2 (last sentence of the 1st para), the examiner has entered that the response to the previous Office Action (of 10/13/2005) was "filed on 04/14/2006." For the record, applicants note that the response was filed on **April 13, 2006**, which is however correctly cited by the examiner on page 7 of the current Office Action.

REQUEST

Applicants submit that the claims are in condition for allowance, and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,

April 13, 2007
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